R E M A R K S

Claims 1-10 are pending in the present application. The Office Action of December 13, 2001, presents the examination of claims 1-6 and 10, claims 7-9 being withdrawn from consideration. Claims 1-6 are amended. No new matter is inserted into the application.

Election/Restriction

In response to the Examiner's Restriction Requirement, Applicants elect Group I, claims 1-6 and 10, without traverse. Applicants reserve the right to pursue a Divisional Application to the non-elected subject matter of Group II, claims 7-9.

Claim Objections

The Examiner objects to claim 5 for being in improper multiple dependent form. Applicants respectfully traverse. Reconsideration of the claim and withdrawal of the instant objection are respectfully requested.

In response to the Examiner's remarks, Applicants amend claim 5 into independent form. Thus, the instant objection is overcome.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-6 and 10 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claims 1, 3, and 10

The Examiner states that claims 1, 3, and 10 are confusing for reciting "residues respectively corresponding to...in the amino acid sequence set forth in SEQ ID NO:1 or an α-amylase having said sequence in an α-amylase having said amino acid sequence."

In response to the Examiner's remarks, Applicants have amended the claims to clarify their meanings. Specifically, claims 1, 3, and 10 are amended to convey that an amino acid substitution or deletion is made in specific positions in SEQ ID NO:1, or that an amino acid substitution or deletion is made in an amino acid sequence having 70% sequence homology to SEQ ID NO:1.

It should be understood by one skilled in the art that the amino acid mutation (i.e., substitution or deletion) may in some cases be the same in SEQ ID NO:1 and an amino acid sequence having 70% sequence homology to SEQ ID NO:1. However, in most cases, the site of the mutation will vary between SEQ ID NO:1 and

the amino acid sequence having 70% sequence homology to SEQ ID NO:1, depending on the variation of the 70% homologous amino acid sequences.

Applicants respectfully submit that the amended claims are fully in compliance with 35 U.S.C. § 112, second paragraph. Thus, the instant rejection is overcome.

Claim 2

The Examiner rejects claim 2 for reciting "residues from the amino terminal in the amino acid sequence set forth in SEQ ID NO:1," which the Examiner asserts is unclear. First, Applicants amend claim 2 to recite,

"A mutant α-amylase obtained by making a substitution of a sequence corresponding to 11 to 100 amino acid residues from the amino terminus of SEQ ID NO: 1 or by making a substitution of a sequence corresponding to 11 to 100 amino acid residues from the amino terminus of an amino acid sequence having at least 70% homology to SEQ ID NO: 1,…."

From the above amendment, it should be clear to one skilled in the art that an 11 to 100 amino acid long substitution from the amino terminus of SEQ ID NO:1 or from the amino terminus of an amino acid sequence having at least 70% homology to SEQ ID NO: 1 is made in order to produce a mutant α-amylase.

Second, Applicants amend the term "replacement" to "substitution" as suggested by the Examiner. Applicants respectfully submit that the amended claim is fully in compliance with 35 U.S.C. § 112, second paragraph. Thus, the instant rejection is overcome.

Claim 6

The Examiner states that the position of SEQ ID NO:1 should be changed. Applicants amend claim 6 so that the term SEQ ID NO:1 is present after each listed amino acid position. Thus, the instant rejection is overcome.

Claims 2-6

The Examiner states that the phrase "replacement of sequence" is confusing as to whether it refers to positions 11 to 100 of SEQ ID NO:1 or all of SEQ ID NO:1. Applicants clarify that this phrase refers to only positions 11 to 100, and have amended the claims accordingly. Thus, the instant rejection is overcome.

Applicants respectfully submit that the amended claims are fully in compliance with 35 U.S.C. § 112, second paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 1, 2, 4-6 and 10 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Svendsen '565 (USP 6,197,565), Mitchinson '499 (USP 5,736,499), Suzuki et al. (*JBC*, 264(32):18933-18938), and Declerck et al. (*Prt. Eng.* 8(10):1029-1037). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The present invention

The claimed subject matter of the present invention includes a mutant α-amylase obtained by making an amino acid substitution or deletion of at least one amino acid residue corresponding to an amino acid residue at a specific position of SEQ ID NO:1, such as the 11^{th} Try residue, the 178^{th} Ala residue, the 188^{th} Glu residue, the 190^{th} Asn residue, the 205^{th} Glu residue, etc., in a sequence comprising SEQ ID NO:1 or having at least 70% sequence homology to SEQ ID NO:1.

Identification of corresponding amino acid positions in a sequence having at least 70% sequence homology to SEQ ID NO:1 requires that the amino acid sequence of a targeted α-amylase is compared with SEQ ID NO:1 by known algorithmic methods, such as the Lippmann-Person method, and subsequently aligned so that the homogeneity of both sequences (i.e. SEQ ID NO:1 and a sequence

having 70% sequence homology to SEQ ID NO:1) are maximized in terms of the conservative amino acid residues shared by them.

The enzymes of the present invention show excellent heat resistance without losing other desirable properties such as resistance to chelating agents. These features of the present invention are recited in the amended claim 1 and supported by the specification, for example on page 1, line 22 to page 3, line 1.

Distinctions between the present invention and Svendsen '565

Svendsen '565 discloses a variant α-amylase having specific amino acid substitutions from the parent SEQ ID NO:4 α-amylase sequence. Svendsen '565 also discloses that any of the Asp or Glu amino acids in positions 185-209 of SEQ ID NO:4 may be replaced with Asn and Gln, respectively.

The Examiner asserts that SEQ ID NO:1 is more than 60% identical to the SEQ ID NO:4 disclosed by Svendsen '565. As such, the Examiner asserts that it is obvious to change positions 190, 205, and 209 of SEQ ID NO:1 when Svendsen '565 discloses amino acid substitutions at the same positions of SEQ ID NO:4.

Applicants respectfully disagree for the following reasons. First, SEQ ID NO:4 as disclosed by Svendsen '565 is not at least 70% homologous to SEQ ID NO:1. As such, SEQ ID NO:4 falls outside the scope of the claims. Second, as the amended claims recite, the mutant α-amylase of the present invention possesses

increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Svendsen '565 fails to disclose a mutant α-amylase with increased heat resistance and maintained resistance to chelating agents.

For these reasons, the present invention is not obvious over Svendsen '565.

Distinctions between the present invention and Mitchinson '499

Mitchinson '499 discloses a variant α-amylase having the deletion or substitution of Asn 188 from *B. licheniformis* α-amylase. Again, the Examiner argues that it would be obvious to change amino acid position 188 based on the disclosure of Mitchinson '499. Applicants respectfully disagree. As noted above, the amended claims recite that the mutant α-amylase of the present invention possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Mitchinson '499 fails to disclose a mutant α-amylase with increased heat resistance and maintained resistance to chelating agents. For these reasons, the present invention is not obvious over Mitchinson '499.

Distinctions between the present invention and Suzuki et al.

Suzuki et al. discloses the deletion of Arg 178 in a *B. licheniformis* α-amylase. Again, the Examiner argues that it would be obvious to change amino acid position 178 based on the disclosure of Suzuki et al. Applicants respectfully disagree. As noted above, the amended claims recite that the mutant α-amylase of the present invention possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Suzuki et al. fails to disclose a mutant α-amylase with increased heat resistance and maintained resistance to chelating agents. For these reasons, the present invention is not obvious over Suzuki et al.

Distinctions between the present invention and Declerck et al.

Declerck et al. discloses the substitution of His 133 and Ala 209 in a *B. licheniformis* α-amylase. The Examiner argues that it would be obvious to change these amino acid positions based on the disclosure of Declerck et al. Applicants respectfully disagree. The amended claims recite that the mutant α-amylase of the present invention possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Declerck et al. fails to disclose a mutant α-amylase with increased heat resistance and maintained

resistance to chelating agents. For these reasons, the present invention is not obvious over Declerck et al.

Conclusion

Applicants respectfully submit that the above amendments render the claims fully in compliance with 35 U.S.C. § 112, second paragraph and that the present application is in a condition for allowance. Early and favorable action of the merits of the present application is thereby respectfully requested.

If there are any minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to April 13, 2002, in which to file a reply to the Office Action. The required fee of $400.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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By _____

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JWB/KLR:gml
Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

The claims have been amended as follows:

1. (Amended) A mutant α-amylase obtained by making a substitution [replacement] or deletion of at least one [residue of] amino acid [residues respectively corresponding to] residue of specific positions in SEQ ID NO:1, or by making a substitution or deletion of at least one amino acid residue corresponding to the above-mentioned amino acid residue in a sequence having at least 70% homology to SEQ ID NO:1,

wherein said at least one amino acid residue is selected from the group consisting of:

the 11th Tyr, 16th Glu, 49th Asn, 84th Glu, 144th Ser, 167th Gln, 169th Tyr, 178th Ala, 188th Glu, 190th Asn, 205th His and 209th Gln [in the amino acid sequence set forth in SEQ ID NO:1 in an α-amylase having said amino acid sequence, or an α-amylase having a homology of at least 70% to said amino acid sequence], and

said mutant α-amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1.

2. (Amended) A mutant α-amylase obtained by making a substitution [replacement] of a sequence corresponding to 11 to 100 amino acid residues from the amino terminus [terminal in the amino acid sequence set forth in] of SEQ ID NO: 1 [in an α-amylase having said amino acid sequence,] or by making a substitution of a sequence corresponding to 11 to 100 amino acid residues from the amino terminus of an amino acid sequence [α-amylase] having [a] at least 70% homology [of at least 70%] to SEQ ID NO: 1, [said]

with another amino acid sequence [by an amino acid sequence of another] that encodes a liquefying α-amylase protein [corresponding to said sequence of the amino acid residues],

wherein said mutant α-amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1.

3. (Amended) The mutant α-amylase according to Claim 2, wherein an amino terminal [a] sequence [corresponding to amino acid residues] from [the] 1st Asp through [to the] 19th Gly [in the amino acid sequence] of SEQ ID NO:1 or an amino terminal sequence corresponding to 1st Asp through 19th Gly of SEQ ID NO:1 of a sequence having at least 70% homology to SEQ ID NO:1, is substituted with [replaced by] an amino acid sequence encoding

[of] another liquefying α-amylase [corresponding to said amino acid sequence].

4. (Amended) The mutant α-amylase according to Claim 2 or 3, wherein said [another] liquefying α-amylase comprises [has the amino acid sequence set forth in] SEQ ID NO:2.

5. (Amended) A mutant α-amylase obtained by introducing at least two mutations [a mutation] into [an α-amylase having the amino acid sequence set forth in] SEQ ID NO:1 or an amino acid sequence [α-amylase] having [a homology of] at least 70% homology to SEQ ID NO:1 [said amino acid sequence],

wherein a first mutation is a [with at least two kinds of] substitution [replacement] or a deletion of at least one amino acid residue selected from the group consisting of the 11th Tyr, 16th Glu, 49th Asn, 84th Glu, 144th Ser, 167th Gln, 169th Tyr, 178th Ala, 188th Glu, 190th Asn, 205th His and 209th Gln [selected from the replacement or deletion of the amino acid residues set forth in Claim 1], and

wherein a second mutation is a substitution [the replacement] of at least one [the] amino [acid] terminal sequence from 1st Asp through 11th Tyr or 100th Asp [sequence set forth in any one of Claims 2 to 4 combined with each other], and

wherein said mutant α-amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1.

6. (Amended) The mutant α-amylase according to Claim 5, wherein said first mutation [the replacement of the amino acid residue] comprises:

the substitution of [replacing] an amino acid residue selected from the group consisting of: [corresponding to] the 11th Tyr [in the amino acid sequence] of SEQ ID NO:1 with [by] Phe, [an amino acid residue corresponding to] the 16th Glu of SEQ ID NO:1 with [by] Pro, [an amino acid residue corresponding to] the 49th Asn of SEQ ID NO:1 with [by] Ser, [an amino acid residue corresponding to] the 167 Gln of SEQ ID NO:1 with [by] Glu, [an amino acid residue corresponding to] the 169th Tyr of SEQ ID NO:1 with [by] Lys, [an amino acid residue corresponding to] the 190th Asn of SEQ ID NO:1 with [by] Phe, [an amino acid residue corresponding to] the 205th His of SEQ ID NO:1 with [by] Arg, or [an amino acid residue corresponding to] the 209th Gln of SEQ ID NO:1 with [by] Val,

and wherein said second mutation [the replacement of the amino acid sequence] comprises:

substituting [replacing] an amino terminal [acid] sequence from [the] 1st Asp through [to the] 19th Gly [in the amino acid sequence] of SEQ ID NO:1 with [by] an amino acid sequence from [the] 1st His to [the] 21st Gly of [in the amino acid sequence set forth in] SEQ ID NO:2.